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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/026,393	12/21/2001	Stephen Quirk	11301-1170 (44039-250928)	1033

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EXAMINER	
SWOPE, SHERIDAN	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 05/25/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/026,393	QUIRK ET AL.	
	Examiner	Art Unit	
	Sheridan L. Swope	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 March 2005 and 28 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *46-61* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *46-61* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's Amendment and Request for Continuing Examination, received April 28, 2005, and Amendment, received March 30, 2005, in response the Final Rejection, mailed January 24, 2004, and the Advisory Action, mailed April 18, 2005, are acknowledged. It is acknowledged that applicants have amended Claims 48, 57, and 61. Claims 46-61 are pending and are hereby reconsidered.

Specification

The specification is objected to for failing to define the abbreviation "SPDP" on page 15, line 3.

The specification is objected to for being unclear in the description of Example 5 on pages 15-16. On page 15, lines 27-28, recitation of "One microgram of protein was mixed with human plasma" is unclear. Is "protein" meant to infer MMP-9, the 11-mer peptide, or some other protein? On page 16, lines 6-7, recitation of "As shown in Figure 7, the antibodies cross reacted with all three MMP forms" is unclear, since Figure 7 only has two data curves and the legend to Figure 7 indicates that the two curves represent proMMP-9 and activated MMP-9. What is meant by "all three MMP forms"?

Claim Rejections - 35 USC § 112-Second Paragraph

The following is a quotation of the second paragraph of 35 USC 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Rejection of Claims 48-50 under 35 USC 112, second paragraph, as being indefinite is maintained. In support of their request that said rejection be withdrawn, Applicants provide the following arguments. Applicant's have amended Claim 48 to recite that the target antibody and

the signal element are "bound" to a particle. But Claim 48 is not intended to distinguish whether the signal element and the antibody are both bound directly and independently to the particle or whether the signal element is bound to the antibody and the signal element/antibody complex is bound to the particle. Claim 48 simply describes the target antibody and the signal element as both being "bound to" a particle. By way of example, Applicants direct the Examiner to page 8, lines 22-26, and page 14, lines 10-11.

These arguments are not found to be persuasive for the following reasons. Neither the specification nor the claims define the phrase "wherein the target antibody and the signal element are bound to a particle" as meaning that the target antibody and the signal element can be bound either independently to the particle or the antibody/signal element, as a complex, can be bound to the particle. The passages at pages 8 and 14 merely define the types of particles encompassed by the recited invention. A person of ordinary skill in the art would not know the metes and bounds of the recited invention. Therefore, rejection of Claims 48-50 under 35 USC 112, second paragraph, as being indefinite is maintained.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 USC 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Rejection of Claims 46-52 and 54-59 under 35 USC 102(b) as being anticipated by Sorsa et al, 1998, for the reasons discussed in the prior action, is maintained.

In support of their request that said rejection be withdrawn, Applicants provide the following arguments in their response of March 30, 2005. The method for diagnosing periodontal disease, as taught by Sorsa et al, does not disclose the presently claimed method for detecting the presence of a proteinase enzyme in a chronic wound (Applicant's emphasis). Sorsa et al is specific the use of a saliva sample, a mouth-rinse sample, or a sample of gingival crevicular fluid to diagnose whether or not a patient has periodontal disease. In contrast, the presently claimed method involves the step of collecting a sample of fluid from a chronic wound. The accepted clinical definition of "chronic wound" does not include oral lesions or periodontal diseases. Rather, these oral lesions resulting from gum disease are defined as "acute" wounds that may worsen without treatment. Chronic wounds and acute wounds are characterized by different sets of biochemical pathway disturbances, and although MMPs may be associated with both chronic wounds and gum disease, the two are quite distinct biochemically. Sorsa et al simply fails to disclose the claimed method for detecting the presence of a proteinase enzyme in a "chronic wound".

In addition, Applicant's provide the following argument in their response of April 28, 2005. "Wound" is clinically defined as "an injury or damage, usually restricted to those caused by physical means with disruption of normal continuity of structures. Synonyms for 'wound' include 'injury' and 'trauma'. Additionally 'chronic' is clinically defined as 'persisting over a long period of time'. In contrast, 'periodontitis' is clinically defined as 'inflammatory reaction of the tissues surrounding a tooth'. (Exhibit A) A chronic wound is quite distinct from periodontis, which is a disease of the tissues surrounding the teeth.

These arguments are not found to be persuasive for the following reasons. Sorsa et al disclose:

> "Periodontal disease comprises a group of inflammatory disorders originating from infections affecting the gingiva (gum) and the alveolar (jaw) bone structures supporting the teeth. The primary cause of periodontal diseases is bacterial plaque attached to the teeth. This causes inflammation of the gum which may result in destruction of the actual tooth-supporting structure and bone" (col 1, lines 21-27).

Thus, periodontal disease, which leads to destruction of the tooth-supporting structure and bone is a chronic condition. Furthermore, a search of the PubMed data-base reveals 2113 articles having both terms "periodontal" and "chronic", 2823 articles having both terms "wound" and "periodontal", and 114 articles having all three terms. See for example:

Taani et al An effective treatment for chronic periodontal abscesses. Quintessence Int. 1996 Oct;27(10):697-9.

Bergstrom et al, Tobacco smoking and chronic destructive periodontal disease. Odontology. 2004 Sep;92(1):1-8.

As described in the Final Rejection of January 24, 2005, Wikesjo et al, 1999 review periodontal wound healing and regeneration and, of special relevance, Graber et al, 1999 provide a review for the role of extracellular matrix proteinases in periodontal wound healing. Therefore, one of skill would know that periodontal disease comprises a chronic wound.

Rejection of Claims 46-52 and 54-59 under 35 USC 102(b) as being anticipated by Golub et al, 2000, for the reasons discussed in the prior action, is maintained. In support of their request that said rejection be withdrawn, Applicants argue that, Golub et al suffers from the same deficiencies noted above with respect to Sorsa et al, i.e., Golub et al is directed to a method for diagnosing periodontal disease, but fails to disclose a method for detecting the presence of a proteinase enzyme in a chronic wound. These arguments are not found to be persuasive for the reasons described above.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 USC 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Rejection of Claims 53, 60, and 61 under 35 USC 103(a) as being unpatentable over Sorsa et al, 1998 in view of Rowe et al, 1999 and further in view of Vu et al, 2000, for the reason set forth in the prior action, is maintained. In support of their request that said rejection be withdrawn, it is believed that Applicants provide the following arguments.

"Dependent claims 47-61 were also rejected under one or both of the above- discussed references and/or the Rowe. et al. and Vu, et al. articles. Applicants respectfully submit that at least for the reasons indicated above relating to independent claim 46, dependent claims 47-61 patentably define over the references) cited. However, Applicants also note that the patentability of dependent claims 47-61 does not necessarily hinge on the patentability of independent claim 46. In particular, some or all of dependent claims 47-61 are believed to possess features that are independently patentable, regardless of the patentability of independent claim 46."

These arguments are not found to be persuasive for the following reasons. First, the Examiner assumes, but it is not clear, that said argument are meant to be relevant to the rejection of Claims 53, 60, and 61 under 35 USC 103(a) as being unpatentable over Sorsa et al, 1998 in view of Rowe et al, 1999 and further in view of Vu et al, 2000. Second, for the reasons indicated above, relating to independent claim 46, regarding Applicant's arguments why Sorsa et al, does not disclose the presently claimed invention, are addressed above. Third, Applicant's do not present their reasons why the patentability of Claims 47-61, and especially Claims 53, 60, and 61, does not hinge on the patentability of Claim 46 or why said claims are believed to possess

features that are independently patentable. Therefore, the Examiner is not able to respond to the undisclosed reasons.

In response to Applicant's argument regarding the semantics of "chronic wound", the following rejection is made. Claims 46-52 and 54-59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Trengove et al, 1999 in view of Sorsa et al, 1998 or Golub et al, 2000. Trengove et al teach a method for detecting metalloprotease in the fluid of a chronic wound using enzymatic assays (Figs 1-3). Trengove et al do not teach a method for detecting metalloproteases in the fluid of chronic wounds using a target antibody, a signal element, and a capture antibody. As described in the First Action on the Merits, mailed July 7, 2004, Sorsa et al teach Sorsa et al teach an immunochromatographic lateral flow method for detecting the matrix metalloproteinase-8 (MMP-8). In said method, a first antibody to MMP-8 is coated onto particles and acts a label that can be detected, for example by its fluorescent or chemiluminescent properties. A sample of an oral swab from an individual having periodontal disease is applied to a reservoir of a capillary support/membrane system. The label/antibody/particles, which are applied to the membrane, migrate by diffusion coming in contact with and binding any MMP-8 in the sample. Further diffusion of the label/antibody/particle/MMP-8 complex brings the complex into contact with a second antibody that has been attached in a zone-like area of the membrane. When the liquid flow, carrying the complex migrates through this zone, label/antibody/particle complexes that have bound protease are bound to the zone. Thus, the zone is detectable if MMP-8 is present in the sample (Abstract; col 22, lines 19-45). As described in the First Action on the Merits, Golub et al, teach (Abstract; col 22, lines 25-52) a method for detecting the matrix metalloproteinase-13 (MMP-13), which uses the same

technology described in Sorsa et al, 1998. It would have been obvious to a person of ordinary skill in the art to use the method of Sorsa et al or Golub et al to detect the presence of metalloproteases in the fluid from chronic wounds. Motivation to do so is derived from the desire to determine which metalloproteases are found in the wound in order to specifically inhibit said metalloproteases, as suggested by Trengove et al (pg 450, parg 9 – pg 451, parg 1). The expectation of success is high, as immunochromatographic lateral flow techniques, using a target antibody, a signal element, and a capture antibody, for analyzing metalloprotease in bodily fluids are known in the art. Therefore, Claims 46-52 and 54-59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Trengove et al, 1999 in view of Sorsa et al, 1998 or Golub et al, 2000.

In response to Applicant's argument regarding the semantics of "chronic wound", the following rejection is made. Claims 53, 60, and 61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sorsa et al, 1998 in view of Trengove et al, 1999 and further in view of Rowe et al, 1999. The teachings of the combination of Sorsa et al and Trengove et al are described above. The combination of Sorsa et al and Trengove et al does not teach a method for detecting a plurality of proteinases in a sample. Rowe et al teach a method for detecting a plurality of proteins in a mixed sample using an array of capture antibodies specific for three different proteins. After incubation with the mixed sample, the binding of each specific protein to its respective capture antibody is detected by a fluorescently-labeled target antibody, which binds to the same specific protein. In this manner, the presence of each of a plurality of proteins in a mixed sample is detected (Fig 4). It would have been obvious to a person of ordinary skill in the art to incorporate the array technique of Rowe et al into the methods of the combination of Sorsa et al and Trengove et al. In such a method, an array of capture antibodies to a plurality of

proteases would be used to bind a plurality of proteases in a mixed sample, which would be detected using fluorescent or chemiluminescent target antibodies to the proteases. Motivation to do so is derived from the fact that a variety of different metalloproteases are involved in the pathology of chronic wounds (Trengove et al, 1999; pg 443, pargs 5-6) and that the array would allow efficient determination of which proteases are present in patient samples. The expectation of success is high, as both the use of capture-antibody arrays to detect a plurality of proteins and the use of capture antibodies to detect proteases are known in the art. Therefore, Claims 53, 60, and 61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sorsa et al, 1998 in view of Trengove et al, 1999 and further in view of Rowe et al, 1999.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan L. Swope whose telephone number is 571-272-0943. The examiner can normally be reached on M-F; 9:30-7 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published application may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on the access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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